

High Production Volume (HPV) Challenge Program

TEST PLAN for HEXAMETHOXYMETHYLMELAMINE

Melamine, hexakis(methoxymethyl)- (CAS # 3089-11-0)

Prepared by

HMMM Coalition

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MELAMINE, HEXAKIS(METHOXYMETHYL)- (CAS # 3089-11-0)	1
A. INTRODUCTION	3
B. GENERAL SUBSTANCE INFORMATION	4
C. MANUFACTURE AND DISTRIBUTION OF HMMM	5
D. USES OF HMMM	6
E. EXPOSURE INFORMATION	6
F. SUMMARY OF AVAILABLE DATA AND TESTING TO BE UNDERTAKEN	6
F. PHYSICAL CHEMICAL DESCRIPTION	11
1. MELTING POINT	11
2. BOILING POINT	12
3. VAPOR PRESSURE	13
4. PARTITION COEFFICIENT	14
5. WATER SOLUBILITY	15
G. ENVIRONMENTAL FATE DATA	16
1. PHOTODEGRADATION	16
2. HYDROLYSIS	17
3. TRANSPORT (FUGACITY)	18
4. BIODEGRADATION	19
H. ECOTOXICITY DATA	20
1a. ACUTE TOXICITY TO FISH	20
1b. ACUTE TOXICITY TO FISH	21
1c. ACUTE TOXICITY TO FISH	22
1d. ACUTE TOXICITY TO FISH	24
2a. ACUTE TOXICITY TO AQUATIC INVERTEBRATES	25
2b. ACUTE TOXICITY TO AQUATIC INVERTEBRATES	26
3. TOXICITY TO AQUATIC PLANTS	27
I. MAMMALIAN TOXICITY	28
1a. ACUTE ORAL TOXICITY	28
1b. ACUTE ORAL TOXICITY	29
1c. ACUTE ORAL TOXICITY	31
1d. ACUTE ORAL TOXICITY	32
1e. ACUTE DERMAL TOXICITY	33
1f. PRIMARY EYE IRRITATION STUDY	35
1g. PRIMARY SKIN IRRITATION STUDY	36
1h. PRIMARY DERMAL IRRITATION STUDY	37
1i. ACUTE INHALATION TOXICITY	38
2. REPEATED DOSE TOXICITY	40
3. DEVELOPMENTAL TOXICITY	43
4. REPRODUCTIVE TOXICITY	43
5. GENETIC TOXICITY	44
a. GENE MUTATIONS	44
b. CHROMOSOMAL ABERRATIONS (In Vitro)	46
c. CHROMOSOMAL ABERRATIONS (In Vivo)	49
J. GENERAL REFERENCE	52

A. INTRODUCTION

The HMMM Coalition has voluntarily agreed to provide information under the U.S. EPA HPV Initiative for melamine, hexakis (methoxy methyl)- (CAS No. 3089-11-0), commonly known as hexamethoxymethylmelamine, and hereafter referred to as HMMM. By participating in this program, the Coalition has agreed to assess the adequacy of existing data on HPV endpoints, design and submit test plans to fill data gaps where necessary and appropriate, provide test results, and prepare summaries of the data characterizing HMMM.

HMMM is a methylated melamine formaldehyde resin used as a crosslinker in thermoset coatings such as beverage can coatings and automotive paint finishes. HMMM cannot be manufactured in pure form and cannot be isolated. Rather, commercial products contain a polymer mixture, and the HMMM itself can be present within the mixture as a monomer (CAS No. 3089-11-0) or as a low-molecular-weight polymer (methylated melamine-formaldehyde polymer, CAS No. 68002-20-0). The exact proportion of HMMM monomer to polymer varies with the manufacturing process, but commercial products are usually about 28-50% HMMM monomer. The balance is primarily the methylated melamine-formaldehyde polymer. Thus, while certain properties can be estimated for a hypothetical 100% monomeric product, the test data presented here are from testing of commercial products containing HMMM in a monomeric/polymeric mixture. For the limited additional testing to be performed pursuant to this Test Plan, the HMMM Coalition will test a commercial product containing the highest amount of HMMM monomer, approximately 50%.

The HMMM Coalition submitting this Test Plan consists of Borden Chemical Inc., Cytec Industries Inc., and UCB, which has assumed the interests of former member Solutia Inc. in HMMM. Solutia manufactured, and UCB now produces, products containing HMMM in polymeric form, and hence is not covered by the HPV program. However, Solutia agreed to provide data regarding its HMMM-containing product. Its low-molecular-weight polymeric HMMM is very similar to the monomeric form of HMMM produced by Borden Chemical and Cytec Industries, and the data are representative of the CAS number listed in the HPV program.

Available data show HMMM has little or no toxicity to aquatic or mammalian organisms. Adequate data are available for almost all of the HPV endpoints:

- Data on physical and chemical properties, including melting point, boiling point, vapor pressure, partition coefficient and water solubility, are estimated from various models, assuming a 100% concentration of HMMM monomer. Measured values for melting point and water solubility will be obtained.
- With regard to environmental fate, HMMM is not predicted to be readily biodegradable, but it is expected to be inherently biodegradable. However, the HMMM Coalition will test for ready biodegradability. HMMM is estimated to have a half-life of minutes in sunlight. Fugacity modeling shows it most likely would be found in soil and to a lesser extent water, rather than air. Hydrolysis potential cannot be estimated from modeling, however, and no data are available on hydrolysis. Thus, the HMMM Coalition will test for hydrolysis.

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- For the ecotoxicological endpoints, adequate data are available for acute toxicity to fish and invertebrates. In two separate tests of bluegill sunfish, no mortality was observed at any doses tested after 96 hours. Similarly, rainbow trout exposed to HMMM showed no mortality after 96 hours at any dose tested. A 48-hour test in daphnia magna also showed no mortality at any dose tested. ECOSAR modeling for daphnia magna produced estimates similar to the bluegill sunfish experimental results. In short, HMMM is not toxic to aquatic organisms. There are no test data for algae, however, and the HMMM Coalition will undertake testing for this endpoint.
 - Respecting the mammalian toxicity endpoints, adequate data exist on almost all of the endpoints, including acute toxicity, repeat dose toxicity, and genotoxicity. Multiple acute tests with oral doses show essentially no toxicity. A 28-day dermal repeat-dose test on HMMM is available. No effects were seen at 250 mg/kg/day, and no effects clearly related to treatment were seen at 750 and 1,000 mg/kg/day. The Ames test showed that HMMM is not mutagenic. While *in vitro* testing of Chinese hamster ovary cell line showed some effect, an *in vivo* chromosome aberration test was negative. Thus, HMMM is not considered clastogenic, and it displays little or no toxicity in mammalian studies.
 - The only mammalian HPV endpoints for which data need to be generated for the HPV program are reproductive and developmental effects. Accordingly, the HMMM Coalition will undertake a combined reproductive/developmental test using OECD Protocol 422.

B. GENERAL SUBSTANCE INFORMATION

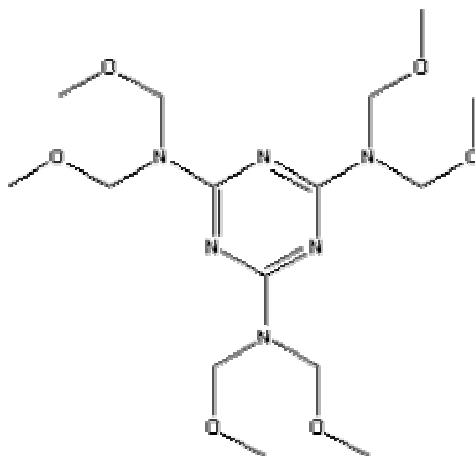
Chemical Name: Melamine, hexakis(methoxymethyl)-

HMMM is formed as a reaction product in addition to several other reaction products when melamine crystal is methylolated and methylated. Commercial products containing HMMM do not exist as a pure material. These products are mixtures that contain HMMM in monomeric and polymeric forms.

Chemical Abstract Service Registry Number: CAS # 3089-11-0

Common Name: HEXAMETHOXYMETHYLMELAMINE (HMMM)

Structural Formula: $C_{15}H_{30}N_6O_6$
Structure:



Molecular Weight: 390.44

Synonyms:

1,3,5-Triazine-2,4,6-triamine, N,N,N',N',N'',N''-hexakis(methoxymethyl)-
 Hexakis(methoxymethyl)melamine
 Hexakis(methoxymethyl)melamin
 hexakis(metoximetil)melamina Hexamethoxy methylmelamine
 1,3,5-Triazine-2,4,6-triamine, N,N,N',N',N'',N''-hexakis(methoxymethyl)-
 2,4,6-[N,N-Bis(methoxymethyl)amino]-1,3,5-triazine
 N,N,N',N',N'',N''-Hexakis(methoxymethyl)-1,3,5-triazine-2,4,6-triamine
 TRIAZINE [1,3,5]-2,4,6-TRIAMINE, N,N,N',N',N'',N''- HEXAKIS(METHOXYMETHYL)-
 HEXAMETHOXYMETHYL MELAMINE

Other Name(s):

1,3,5-Triazine-2,4,6-triamine, N,N,N',N',N'',N''-hexakis(methoxymethyl)-
 Hexa(methoxymethyl)melamine
 Hexamethyl methylolmelamine
 Hexamethylolmelamine hexamethyl ether
 Melamine, hexakis(methoxymethyl)-
 N,N,N',N',N'',N''-Hexakis(methoxymethyl)-1,3,5-triazine-2,4,6-triamine
 Pidifix 330

C. MANUFACTURE AND DISTRIBUTION OF HMMM

Commercial methylated melamine formaldehyde resins are complex mixtures of dimers, trimers and higher oligomers. No direct industrial synthesis of HMMM has been reported. HMMM-containing resins are formed by methylation of melamine with formaldehyde in the presence of acid or alkali, followed by methylation with methanol in the presence of acid.

HMMM containing resins are not sold directly to the consumer market. This material is reacted into the coatings in which they are added, limiting potential exposure in the finished consumer products.

HMMM is not sold as 100% HMMM. It is generally a mixture of HMMM, dimers and higher oligomers, and a smaller amount of less methylolated/methylated species. The typical commercial form is either a solid wax or liquid at ambient temperatures. The solid wax can be heated back to liquid form.

D. USES OF HMMM

HMMM-containing resins are used as crosslinkers in thermoset coatings. Their principal function is to crosslink the molecules of the primary film-forming vehicle in a coating, in order to build a three-dimensional thermoset polymer network with high performance properties. This involves the reaction of the functional groups (such as the methoxymethyl groups on HMMM) to the complementary reactive groups on the vehicle, typically in the presence of an acid catalyst. This imparts characteristics such as hardness and mar resistance to the coating finishes. The thermoset coating formed from HMMM-containing resins is considered excellent for solvent resistance, chemical resistance and exterior durability. Examples of applications are automotive paint finishes and beverage can coatings. HMMM is also used in methylated melamine formaldehyde resins, which are approved by FDA for use in food packaging.

E. EXPOSURE INFORMATION

HMMM resin is the predominant crosslinking agent for thermoset coatings. Thermoset coatings undergo chemical reactions during the curing process so that the molecular weight is built up and crosslinking takes place. Thus, upon curing, the parent methylated melamine formaldehyde material is no longer present.

The only potential routine worker contact comes from sampling procedures for quality control, and in some instances, during packaging. Exposure would be by skin contact. Inhalation exposure is extremely low due to the use of ventilation and the material's low vapor pressure. Ingestion would not be expected.

No consumer exposure would be expected, as HMMM would not be present in the coated products.

F. SUMMARY OF AVAILABLE DATA AND TESTING TO BE UNDERTAKEN

Data on HMMM are already available for almost all of the HPV endpoints. The following paragraphs briefly summarize the available data, which are then presented in tabular form and in robust summaries.

Data on physical and chemical properties, including melting point, boiling point, vapor pressure, partition coefficient and water solubility, are estimated from various models, assuming a 100% concentration of HMMM. Based on these results, measured values will be obtained for melting point and water solubility. With regard to environmental fate, HMMM is not predicted to be readily biodegradable, but it is expected to be inherently biodegradable. The HMMM Coalition will test for ready biodegradability. HMMM is estimated to have a half-life of minutes in sunlight. Fugacity modeling shows it most likely would be found in soil and to a lesser extent

water, rather than air. Hydrolysis potential cannot be estimated from modeling, however, and no data are available on hydrolysis. Thus, the HMMM Coalition will test for hydrolysis.

Commercial products containing HMMM have been tested for ecotoxicological endpoints and for mammalian endpoints.

For the ecotoxicological endpoints, adequate data are available for acute toxicity to fish and invertebrates. In two separate tests of bluegill sunfish, no mortality was observed at any doses tested after 96 hours. Similarly, rainbow trout exposed to HMMM showed no mortality after 96 hours at any dose tested. A 48-hour test in daphnia magna also showed no mortality at any dose tested. ECOSAR modeling for daphnia magna produced estimates similar to the bluegill sunfish experimental results. There are no data available evaluating potential toxicity to algae, however, and the HMMM Coalition will undertake such testing to fulfill this endpoint.

Respecting the mammalian toxicity endpoints, adequate data exist on almost all of the endpoints, including acute toxicity, repeat dose toxicity, and genotoxicity. Multiple acute tests with oral doses show essentially no toxicity. A 28-day dermal repeat-dose test on HMMM is available. No effects were seen at 250 mg/kg/day. At 750 and 1,000 mg/kg/day, there were some effects on organ weights in males and liver enzyme values in females that were not clearly related to treatment. No clinical signs of dermal irritation or toxicity were observed. There were no macro or microscopic changes in any of the male or female reproductive organs.

The Ames test showed that HMMM is not mutagenic. Although *in vitro* testing of Chinese hamster ovary cell line showed some effect, an *in vivo* chromosome aberration test (bone marrow cytogenetics rat metaphase analysis) was negative. Thus, HMMM is not considered clastogenic, and it displays little or no toxicity in mammalian studies.

The only mammalian HPV endpoints for which data need to be generated for the HPV program are reproductive and developmental effects. Accordingly, the HMMM Coalition will undertake a combined reproductive/developmental test using OECD Protocol 422.

The tables below summarize the available data and the planned testing. The tables are followed by robust summaries of the existing data. A legend for the Klimisch codes is set out at the end of the robust summaries.

For the limited additional testing to be undertaken, the test material will be a Cytec Industries commercial product, with the following composition: ~52% HMMM monomer (CAS No. 3089-11-0), ~47% methylated melamine-formaldehyde polymer (CAS No. 68002-20-0), <1% methanol, ~0.15% formaldehyde and <0.1% water. As noted above, HMMM cannot be produced in isolation. This commercial product is representative of the HMMM in commerce.

TABLE 1 SUMMARY OF AVAILABLE DATA ON HMMM

CAS# 3089-11-0	Study Date	Results	Data Acceptable
Physical/Chemical Characteristics*			
Melting Point	2002	188.40 °C	No#
Boiling Point	2002	448.20 °C	Yes
Vapor Pressure	2002	1.06 x 10⁻⁸ mm Hg @ 25 °C	Yes
Partition Coefficient	2002	Log K_{ow} = 1.61	Yes
Water Solubility	2002	149.3 mg/L @ 25 °C	No#
Environmental Fate*			
Photodegradation	2002	For reaction with hydroxyl radical, predicted rate constant = 323.5521 x 10 ⁻¹² cm ³ /molecule-sec Predicted half-life = 23.802 minutes	Yes
Hydrolysis		No data	No Data
Fugacity	2002	Predicted distribution using Level III Fugacity Model: Air: 0.0000645% Water: 36.1% Soil: 63.8% Sediment: 0.0996%	Yes
Biodegradation	2002	Inherently biodegradable	No#
Ecotoxicity			
Acute Toxicity to Fish	1993 1984 2002 1983	Lepomis macrochirus: LC50 (96 hr) = 603.1 mg/L LC50 (96 hr) = >1,000 mg/L LC50 (96 hr) = 673.2 (estimated) Salmo gairdneri: LC50 (96 hr) = >1,000 mg/L	Yes Yes Yes Yes
Acute Toxicity to Invertebrates	1983 2002	Daphnia magna LC50 (48hr) = >1,000 mg/L LC50 (48hr) = 702.2 mg/L (estimated by ECOSAR)	Yes Yes
Acute Toxicity to Algae		No data	No data

Mammalian Toxicity			
Acute Toxicity			
Oral LD50 (rat)	2001	oral LD50 (rat) = 2.0 g/kg	Yes
Oral LD50 (rat)	1984	oral LD50 (rat) = 1.8 g/kg	Yes
Oral LD50 (rat)	1976	oral LD50 (rat) = 7.4 g/kg	Yes
Oral LD50 (rat)	1960	oral LD50 (rat) = >5 g/kg	No
Dermal LD50 (rabbit)	1976	dermal LD50 (rat) = >7.9 g/kg	Yes
Inhalation LC50	1976	6-hour inhalation LC50 = >0.6 mg/L	No
Primary Eye Irritation	1976	Slight Eye Irritant	Yes
Primary Skin Irritation	1976	Non-Irritating to Skin	No
Primary Skin Irritation	1988	Mild to Non-Irritating to Skin	Yes
Repeat Dose Toxicity			
28-Day Dermal (rat)	1990	NOEL = 250 mg/kg/day (dermal) NOAEL = 1000 mg/kg/day	Yes
Developmental Toxicity		No data	No Data
Reproductive Toxicity		No data	No Data
Genetic Toxicity:			
Gene Mutations	1988	Negative	Yes
Chromosomal Aberration			
In Vitro (CHO Cell Assay)	1989	Positive (In Vitro)	Yes
In Vivo (Bone Marrow	1989	Negative (In Vivo)	Yes
Cytogenetics)			

* Estimated by modeling for hypothetical 100% concentration of HMMM.

Measured values for melting point, water solubility and ready biodegradability will be obtained.

TABLE 2 SUMMARY OF TESTING

CAS # 3089-11-0	Data Available	Data Acceptable	Testing Required
Study	Y/N	Y/N	Y/N
Physical/Chemical Characteristics			
Melting Point	Y	Y/N	YES
Boiling Point	Y	Y	N
Vapor Pressure	Y	Y	N
Partition Coefficient	Y	Y	N
Water Solubility	Y	Y/N	YES
Environmental Fate			
Photodegradation	Y	Y	N
Hydrolysis	N	No data	YES
Fugacity	Y	Y	N
Biodegradation	Y	Y/N	YES
Ecotoxicity			
Acute Toxicity to Fish	Y	Y	N
Acute Toxicity to Invertebrates	Y	Y	N
Acute Toxicity to Algae	N	No data	YES
Mammalian Toxicity			
Acute Toxicity	Y	Y	N
Repeat Dose Toxicity	Y	Y	N
Developmental Toxicity	N	No data	YES
Reproductive Toxicity	Y	No data	YES
Genetic Toxicity: Gene Mutations	Y	Y	N
Genetic Toxicity: Chromosomal Aberration	Y	Y	N